

Application No. 09/698,323
Amendment dated November 12, 2007
Reply to Office Action of July 12, 2007

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Docket No.: 47624DRV(71417)

AMENDMENTS TO THE CLAIMS

The below listing of claims will replace all prior versions, and listings, of claims in the application:

1-49. (Canceled)

50. (Previously presented) A method for inducing formation of new blood vessels in a mammal having chronic or acute ischemia, wherein the method comprises administering to the mammal an effective amount of a vascular endothelial growth factor (VEGF) and a granulocyte-macrophage colony stimulating factor (GM-CSF), or an effective fragment thereof, wherein the mammal is a rodent or a primate.

51. (Canceled)

52. (Currently amended) A method for inducing formation of new blood vessels in a mammal having chronic or acute ischemia, wherein the method comprises administering to the mammal an amount of vascular endothelial growth factor (VEGF) and GM-CSF sufficient to increase frequency of endothelial progenitor cells (EPC) in the mammal.

53-54. (Canceled)

55. (Previously presented) The method of claim 50 or 52, wherein the amount of VEGF or GM-CSF administered to the mammal is sufficient to increase blood vessel length in the mammal.

56. (Previously presented) The method of claim 55, wherein the increase in blood vessel length is at least about 5% as determined by a standard blood vessel length assay.

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57. (Previously presented) The method of claim 50 or 52, wherein the amount of VEGF or GM-CSF administered to the mammal is further sufficient to increase blood vessel diameter in the mammal.

58. (Previously presented) The method of claim 56, wherein the increase in blood vessel diameter is at least about 5% as determined by a standard blood vessel diameter assay.

59. (Previously presented) The method of claim 50 or 52, wherein the amount of factor administered to the mammal is sufficient to increase EPC differentiation following tissue ischemia.

60. (Previously presented) The method of claim 59, wherein the increase in EPC differentiation is at least about 20% as determined by a standard hindlimb ischemia assay.

61. (Previously presented) The method of claim 50 or 52, wherein the amount of administered factor is sufficient to increase neovascularization by at least about 5% as determined by a standard cornea micropocket assay.

62. (Previously presented) The method of claim 50 or 52, wherein the amount of administered factor is sufficient to increase EPC incorporation into foci.

63. (Previously presented) The method of claim 62, wherein the increase in EPC incorporation into foci is at least about 20% as determined by a standard rodent bone marrow (BM) transplantation model.

64. (Canceled)

65. (Previously presented) The method of claim 63, wherein the mammal has ischemic tissue which comprises tissue from a limb, graft, or organ.

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66. (Previously presented) The method of claim 65, wherein the tissue is associated with the circulatory system or the central nervous system.

67. (Previously presented) The method of claim 65, wherein the tissue is heart or brain tissue.

68. (Previously presented) The method of claim 50 or 52, wherein the VEGF or GM-CSF is co-administered with at least one angiogenic protein.

69. (Canceled)

70. (Previously presented) The method of claim 68, wherein the angiogenic protein is acidic fibroblast growth factor (aFGF), epidermal growth factor (EGF), transforming growth factor (TGF)- α , TGF- β , platelet-derived endothelial growth factor (PD-ECGF), platelet-derived growth factor (PDGF), tumor necrosis factor α , hepatocyte growth factor (HGF), insulin like growth factor (IGF), erythropoietin, colony stimulating factor (CSF), macrophage-CSF (M-CSF), angiopoietin-1 (Ang1) or nitric oxide synthase (NOS); or a fragment thereof.

71. (Canceled)

72. (Currently amended) A method for preventing or reducing the severity of blood vessel damage in a mammal having chronic or acute ischemia, wherein the method comprises administering to the mammal an effective amount of VEGF and granulocyte macrophage-colony stimulating factor (GM-CSF); and exposing the mammal having the chronic or acute ischemia to conditions conducive to damaging the blood vessels, the amount of VEGF and GM-CSF being sufficient to prevent or reduce the severity of the blood vessel damage in the mammal.

73. (Previously presented) The method of claim 72, wherein the conditions conducive to the blood vessel damage are an invasive manipulation or ischemia.

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74. (Previously presented) The method of claim 73, wherein the invasive manipulation is surgery.

75. (Previously presented) The method of claim 73, wherein the ischemic is associated with at least one of infection, trauma, graft rejection, cerebrovascular ischemia, renal ischemia, pulmonary ischemia, limb ischemia, ischemic cardiomyopathy, or myocardial ischemia.

76. (Previously presented) The method of claim 72, wherein the GM-CSF is administered to the mammal at least about 12 hours before exposing the mammal to the conditions conducive to damaging the blood vessels.

77. (Previously presented) The method of claim 76, wherein the GM-CSF is administered to the mammal between from about 1 to 10 days before exposing the mammal to the conditions conducive to damaging the blood vessels.

78. (Previously presented) The method of claim 76, wherein the method further comprises administering the GM-CSF to the mammal following the exposure to the conditions conducive to damaging the blood vessels.

79-83. (Canceled)

84. (Currently amended) A method for inducing formation of new blood vessels in a mammal having chronic or acute ischemia, wherein the method comprises administering to the mammal an effective amount of a vascular endothelial growth factor (VEGF) and granulocyte-macrophage colony stimulating factor (GM-CSF) ~~or GM-CSF~~, or an effective fragment thereof and increasing endothelial progenitor cell (EPC) frequency by at least about 20% as determined by a standard EPC isolation assay, wherein the mammal is a rodent or a primate.